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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,751	02/07/2002	Shirley Wu Hunter	2618-17-C4-PUS-2	2578

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/071,751	HUNTER ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 65-76 are pending in the application.

[2] Applicants' amendment to the claims, filed October 07, 2004, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims in the instant application.

[3] Applicants' amendment to the specification, filed October 07, 2004, is acknowledged.

[4] Applicant's arguments filed October 07, 2004 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Priority

[6] Applicants' claim to domestic priority under 35 U.S.C. 120 to US non-provisional applications 09/171,156, 08/630,822, 08/847,001, and 08/319,590 is acknowledged.

[7] It is noted that applicants claim priority to application PCT/US97/05959. However, the sequence of $Pfsp_{155}$ (SEQ ID NO:62) of the instant application is not supported by application PCT/US97/05959 as $Pfsp_{155}$ of application PCT/US97/05959 (corresponding to SEQ ID NO:62; see page 24, lines 10-11 of

WO 97/37676) is not identical to $Pfsp_{155}$ (SEQ ID NO:62) of the instant application (See Appendix A of the Office action mailed May 14, 2004).

Claim Objection

[8] Claim 65 is objected to in the recitation of "6 amino sequence" and should be replaced with, for example, "6 amino acid sequence."

Claim Rejections - 35 USC § 112, Second Paragraph

[9] Claims 65-68, 70, and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

[a] Claims 65 (claim 68 dependent therefrom) and 66-67 are confusing in that claim 65 recites "at least 6 contiguous amino acid sequence" followed by the recitation of "said 6 amino [acid] sequence" in claims 65-67. In order to clarify the claims, it is suggested that applicants amend "said 6 amino [acid] sequence" to "said at least 6 amino [acid] sequence."

[b] Claims 67 and 75 are indefinite in the recitation of "hypersensitive response" and "an animal known to be hypersensitive." It is unclear from the specification and the claims as to how one of skill determines the scope of immune responses that are considered to be "hypersensitive" from those that are considered to be non-hypersenstitive. Further, it is unclear as to how one of skill determines the scope of those animals that are considered to be "known to be

hypersensitive" from those that are not known. It is suggested that applicants clarify the meaning of the claims.

[c] Claim 68 is unclear because claim 68 limits the portion of claim 65 to at least 38 contiguous amino acids of SEQ ID NO:62, however, it is unclear as to whether the 38 contiguous amino acids of SEQ ID NO:62 elicit an immune response or if only "said 6 amino [acid] sequence" of SEQ ID NO:62 as recited in line 3 of claim 65 elicits an immune response. It is suggested that applicants clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

[10] The new matter rejection of newly added claims 68 and 76 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth at item [11] of the Office action mailed May 14, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENTS: Applicants argue the specification has been amended to properly claim priority to US Patent 5,795,862, which discloses SEQ ID NO:6, a 38 amino acid fragment of SEQ ID NO:62. In response to the examiner's argument that the limitation of "38 contiguous amino acids" of SEQ ID NO:62 is not supported by the disclosure of SEQ ID NO:6, a specific 38 amino acid fragment of SEQ ID NO:62, applicants argue the specification discloses that portions of SEQ ID NO:62 are embodiments of the claimed invention and are supported by the specification. Applicants' argument is not found persuasive.

The examiner maintains the position that the disclosure of SEQ ID NO:6 in application 08/487,001, which issued as US patent 5,795,862 does not provide support for all fragments of at least 38 amino acids as recited in the claims. First, it is noted that US non-provisional application 08/487,001 is not incorporated by reference. MPEP 608.01(p) states, "[f]or the incorporation by reference to be effective as a proper safeguard, the incorporation by reference statement must be filed at the time of filing of the later-filed application. An incorporation by reference statement added after an application's filing date is not effective because no new matter can be added to an application after its filing date (see 35 U.S.C. 132(a)." If applicants attempt to incorporate the disclosure of US patent 5,795,862 by reference, it is noted that this is an improper incorporation by reference.

Even assuming *arguendo* US non-provisional application 08/487,001 was properly incorporated by reference at the time of the invention, it is noted that applicants' disclosure does not specifically disclose a range of amino acids of at least 38 contiguous amino acids of SEQ ID NO:62. As such, this limitation is new matter.

[11] The written description rejection of newly added claims 65-68 and 70 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth at item [12] of the Office action mailed May 14, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENTS: Applicants argue that they envisioned the use of fragments of at least 6 amino acids of SEQ ID NO:62 and that, while every

possible fragment of SEQ ID NO:62 is not disclosed, the disclosure of SEQ ID NO:62 inherently discloses all possible fragments as well. Applicants argue a functional limitation has been added and that because the functional activity is allegedly limited to the fragment of SEQ ID NO:62, the flanking residues are irrelevant. Applicants' argument is not found persuasive.

The examiner maintains the position that the single representative species of SEQ ID NO:62 fails to represent the entire genus of claimed polypeptides. It should be noted that, while the examiner agrees that all possible fragments of SEQ ID NO:62 have been disclosed, the claims are not so limited to fragments of SEQ ID NO:62. Unlike claims 65-68 and 70, claims 72-76 are *limited to fragments of SEQ ID NO:62*, wherein the fragment is at least 6 or 38 contiguous amino acids of SEQ ID NO:62. However, the polypeptide of claims 65-68 is a polypeptide that *comprises* at least 6 amino acids of SEQ ID NO:62. While it is acknowledged that the "at least 6 contiguous amino acid sequence" is "functionally" limited to those that elicit an immune response to a protein comprising SEQ ID NO:62, this limitation does not itself limit the function of the protein as one of skill in the art would expect a fragment of a given protein to likely be able to elicit an antibody that would bind that protein. In this case, the genus of claimed proteins is widely variant with respect to both structure and function. With regard to structure, the genus encompasses any protein that comprises at least 6 contiguous amino acids of SEQ ID NO:62. With regard to function, the genus encompasses proteins having widely variant functions. As evidence of such variability within the genus, it is noted that species

encompassed by the genus include (but are not limited to) such widely variant proteins as an RNA recognition motif-type RNA-binding protein (Appendix A), an acetolactate synthase polypeptide (Appendix B), and a ribosomal protein S6 kinase II polypeptide homolog (Appendix C). In this case, the single representative species of SEQ ID NO:62 fails to represent all species encompassed by the genus of claimed proteins.

[12] The scope of enablement rejection of new claims 65-68 and 70 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record as set forth at item [14] of the Office action mailed May 14, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENTS: Addressing the scope of the claims, applicants argue that while a large number of proteins may comprise a fragment of SEQ ID NO:62, not all of these proteins will have the activity of eliciting the recited immune response. Applicants' argument is not found persuasive.

There is no requirement that the protein comprising the recited portion of SEQ ID NO:62 elicit an immune response against a protein comprising SEQ ID NO:62. Instead, it is the portion of SEQ ID NO:62 itself that elicits the immune response. In this way, the "function" of the portion of SEQ ID NO:62 does not limit the overall function of the claimed polypeptide in any way as a skilled artisan would expect a fragment of a given protein, *i.e.*, SEQ ID NO:62, to elicit an immune response to that protein. In this case, the claims are so broad as to encompass a vast number of proteins having any function, including an RNA recognition motif-type RNA-binding protein (Appendix A), an acetolactate

synthase polypeptide (Appendix B), and a ribosomal protein S6 kinase II polypeptide homolog (Appendix C).

Addressing the guidance and working examples, applicants argue that US Patent 5,795,862 discloses two additional working examples of the claimed polypeptides, *i.e.*, SEQ ID NO:25 and 35 of that patent. Applicants' argument is not found persuasive.

It is noted that, in addition to SEQ ID NO:25 and 35 of US Patent 5,795,862, the prior art recognizes at least two additional working examples of the claimed proteins as shown in Appendices A and B. However, these additional working examples fail to provide guidance for making and using all proteins as broadly encompassed by the claims as evidenced by Appendices A-C. Moreover, it is noted that the specification fails to disclose the use of all polypeptides as encompassed by the claims. For example, the specification fails to provide guidance for using the RNA-binding protein, acetolactate synthase polypeptide, and the ribosomal protein S6 kinase II polypeptide homolog as shown in Appendices A, B, and C, respectively.

Addressing the unpredictability in the art, applicants argue the claims do not encompass proteins comprising SEQ ID NO:62 fragments that have been altered by substitution or insertion. Applicants argue the claims are limited to a well-defined, finite number of fragments and the specification discloses how to test such fragments for activity. Applicants' argument is not found persuasive.

Contrary to applicants' argument, the claims encompass any sequence of amino acids that comprises fragments of SEQ ID NO:62, including substitution

and insertion mutants thereof, as long as the protein comprises a fragment of SEQ ID NO:62 (see Appendices A, B, and C). In addition to the reasoning regarding the unpredictability as stated in a previous Office action, it is noted that the ability of an antibody to bind a particular epitope within a polypeptide is dependent upon the amino acid sequence of the polypeptide and, if the polypeptide is in its native state, *i.e.*, non-denatured, the resulting conformation acquired by the amino acid sequence (see Abaza et al. *J Protein Chem* 11:433-444 who teach that "the reaction of a protein antigen with its antibodies is influenced by conformational changes" (page 436, left column, bottom to right column, top)). It is highly unpredictable as to which alterations in a protein's amino acid sequence can be made with an expectation of maintaining the ability of an antibody to bind the altered polypeptide sequence. The state of the art provides evidence for the high level of unpredictability that an antibody, *e.g.*, an antibody that binds SEQ ID NO:62, will bind to an altered polypeptide sequence, *e.g.*, a polypeptide comprising a fragment of SEQ ID NO:62, such as those polypeptides shown in Appendices A-C. For example, Abaza et al. (*J Protein Chem* 11:433-444) teach that alterations outside of the boundaries of an antigenic site can significantly affect antibody binding (page 443, right column to page 444, left column). As such, there is a high level of unpredictability that all polypeptides comprising a fragment of SEQ ID NO:62 as encompassed by the claims will have the desired utility/activity of eliciting an antibody that binds to SEQ ID NO:62.

Addressing the amount of experimentation required, applicants argue that it is not undue experimentation to screen all polypeptides encompassed by the claims for those having the desired activity. Applicants' argument is not found persuasive.

As stated previously, in view of the broad scope of the claimed proteins as evidenced above, the lack of guidance and working examples as evidenced above, the unpredictability in the art as evidenced above, the experimentation required to screen all polypeptides comprising a fragment of SEQ ID NO:62 as encompassed by the claims, is not routine. At least for these reasons and the reasons of record, undue experimentation is required to make and use the broad scope of claimed proteins.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

[13] In view of applicants' amendment to the specification to perfect a claim to domestic priority under 35 U.S.C. 120 and 121, the rejection of claims 43-45, 57-58, and 61-62 (and corresponding new claims 65-68 and 70) under 35 U.S.C.

102(e) as being anticipated by Frank et al. (US Patent 5,795,862) as set forth at item [16] of the Office action mailed May 14, 2004, is withdrawn.

[14] In view of applicants' amendment to the specification to perfect a claim to domestic priority under 35 U.S.C. 120 and 121, the rejection of claims 43-45, 57-58, and 61-62 (and corresponding new claims 65-68 and 70) under 35 U.S.C. 102(e) as being anticipated by Frank et al. (US Patent 5,646,115) as set forth at item [17] of the Office action mailed May 14, 2004, is withdrawn.

[15] Claims 65-67 and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by GenPept Accession Number S15004 (see Appendix B). This rejection is necessitated by amendment. Claim 65 is drawn to an isolated protein comprising at least 6 amino acids of SEQ ID NO:62, wherein the at least 6 amino acids elicit an immune response against a protein comprising SEQ ID NO:62. Claims 66-67 limit the fragment of SEQ ID NO:62 to a fragment that forms an immunocomplex or a fragment that induces a hypersensitive response. Claim 70 is drawn to a composition comprising the protein of claim 65.

S15004 teaches a polypeptide comprising at least 6 amino acids of SEQ ID NO:62, *i.e.*, amino acids 106-112 of SEQ ID NO:62. This anticipates claims 65-67 and 70 as written.

Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the protein of the prior art does not possess the same material structural and functional characteristics of the claimed protein).

See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

Claim Rejections – Double Patenting

[16] The obviousness-type double patenting rejection of new claim 70 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 of Frank et al. (US Patent 5,795,862) is maintained for the reasons of record as set forth at item [18] of the Office action mailed May 14, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENTS: Applicants submit that the appropriate terminal disclaimer will be submitted upon resolution of all other issues. Applicants' argument is acknowledged and, as a terminal disclaimer has not been received as of the drafting of the instant Office action, the rejection is maintained.

[17] The obviousness-type double patenting rejection of new claims 65 and 70 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4 of Frank et al. (US Patent 5,646,115) is maintained for the reasons of record as set forth at item [19] of the Office action mailed May 14, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENTS: Applicants submit that the appropriate terminal disclaimer will be submitted upon resolution of all other issues. Applicants' argument is acknowledged and, as a terminal disclaimer has not

been received as of the drafting of the instant Office action, the rejection is maintained.

[18] The obviousness-type double patenting rejection of new claim 70 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 14 and 20-21 of US non-provisional Patent Application 10/271,344 is maintained for the reasons of record as set forth at item [20] of the Office action mailed May 14, 2004 and for the reasons stated below.

RESPONSE TO ARGUMENTS: Applicants submit that the appropriate terminal disclaimer will be submitted upon resolution of all other issues. Applicants' argument is acknowledged and, as a terminal disclaimer has not been received as of the drafting of the instant Office action, the rejection is maintained.

Conclusion

[19] Status of the claims:

- Claims 65-76 are pending.
- Claims 65-68, 70, and 75-76 are rejected.
- Claim 69 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
- Claims 71-74 appear to be in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.**

See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

11-10-04

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1652